## IN THE SPECIFICATION

Please amend the paragraph beginning on page 1, line 16 as follows:

Cystic fibrosis (CF) is caused by a genetic mutation in the cystic fibrosis transmembrane conductance regulator (CFTR), and is the most common genetic disorder in the Caucasian population. CFTR is a chloride channel that localizes to the apical membrane of epithelial cells in many organs such as the lung. The channel is activated by cyclic AMP (cAMP) and regulated by PKA- and PKC-dependent phosphorylation. In addition to functioning as a chloride channel, CFTR has also been shown to regulate several other ion channels at the cell surface (Jiang et al., 1998), including the epithelial amiloride-sensitive sodium channel (ENaC) (Stutts et al. ~~Stults et al.~~, 1997; Donaldson et al., 2002), outward rectifying chloride channel (ORCC) (Gabriel et al., 1993; Schwiebert et al., 1998), renal potassium channel (ROMK2) (Cahill et al., 2000), and the calcium activated chloride channel (Kunzelmann et al., 1997).

Please amend the paragraph beginning on page 13, line 1 as follows:

Figure 2. *In vivo* enhancement of rAAV transduction with DOXIL® [[Doxil]]. Male Balb/c mice intravenously administered DOXIL® [[Doxil]] were endotracheally instilled with 1 x $10^{11}$ DRP AAV2FLAG-Luc (01:004). A) Effect on rAAV lung transduction. B) Effect on rAAV tracheal and bronchial transduction.

Please amend the paragraph beginning on page 28, line 1 as follows:

Cysteine protease inhibitors within the scope of the invention include the cystatins, e.g., cystatin B or cystatin C, antipain, leupeptin, E-64, E-64c, E-64d, KO2 (Wacher et al., 1998), LLnL, Z-LLL, CBZ-Val-Phe-H, cysteine protease inhibitors such as those disclosed in U.S. Patent Nos. U.S. Patent No. 5,607,831, 5,374,623, 5,639,732, 5,658,906, 5,714,484, 5,560,937, 5,374,623, 5,607,831, 5,723,580, 5,744,339, 5,827,877, 5,852,007, and 5,776,718, JP 10077276, JP 8198870, JP 8081431, JP 7126294, JP 4202170, WO 96/21006 and WO 96/40737 as well as

Cdz-Leu-Leu-norvalinal (MG115), carbobenzoxy-isoleucyl-(gamma)-t-butyl-L-glutamyl-L-alanyl-L-leucinal (PSI), N-acetyl-leu-leunorleucinal (ALLN),
MLN519 (Millennium Pharmaceuticals), [(1R)-3-methyl-1-[[(2S)-3-phenyl-2-[(pyrazinylcarbonyl)- amino]propanoyl]amino]butyl]boronic acid (PS-341, known generically as "bortezomib;" trade name VELCADE® ~~Velcade~~; Millennium Pharmaceuticals),
Z-Ile-Glu(OtBu)-Ala-Leu-H, SRI6975 (2 acetylpyridine N phenylguanylhydrazonedihydrochloride, ALLM (N-acetyl-Leu-Leu-methional), clasto-lactacystin beta lactone, as well as proteasome inhibitors disclosed in Iqbal et al. (1995) and Lee et al. (2000), the disclosures of which are specifically incorporated by reference herein.

Please amend the paragraph beginning on page 43, line 14 as follows:

These formulations can contain pharmaceutically acceptable vehicles and adjuvants which are well known in the prior art. It is possible, for example, to prepare solutions using one or more organic solvent(s) that is/are acceptable from the physiological standpoint, chosen, in addition to water, from solvents such as acetone, ethanol, isopropyl alcohol, glycol ethers such as the products sold under the name DOWANOL® ~~"Dowanol"~~, polyglycols and polyethylene glycols, $C_1$-$C_4$ alkyl esters of short-chain acids, preferably ethyl or isopropyl lactate, fatty acid triglycerides such as the products marketed under the name "Miglyol", isopropyl myristate, animal, mineral and vegetable oils and polysiloxanes.

Please amend the paragraph beginning on page 70, line 18 as follows:

B. HeLa cells were selected to screen for additional agents that enhance rAAV transduction, although any cell strain or line; or primary cells, may be employed. Agents were selected from various classes, such as anti-inflammatories (e.g., dexamethasone and cyclosporin A), NSAIDs (e.g., ibuprofen), β-adrenergics (e.g., albuterol), antibiotics (e.g., ciprofloxacin, colison, gentamycin, tobramycin, and epoxomycin), lipid lowering agents (e.g., lovastatin, simvastatin and eicosapentaenoic acid), food additives (e.g., tannic acid), viral protease inhibitors (e.g., NORVIR®, KALETRA® and VIRACEPT® ~~Norvir, Kaletra, and Viracept~~), chemotherapeutics (e.g., aclacinomycin A, doxorubicin, DOXIL® [[doxil]], camptothecin, taxol and cisplatin) and

protease inhibitors (e.g., chymostatin, bestatin and chloroquine). The range of concentrations of the agents to be tested were selected based on solubility profiles, toxicity profiles and/or concentrations previously employed *in vivo*.

Please amend the paragraph beginning on page 71, line 20 as follows:

It should be noted with respect to simvstatin and the lovastatin, that these drugs are formulated as prodrugs and conversion to the activated open ring forms was not confirmed which may have contribute to the negative results. Similarly, the liposomal formulation of doxorubicin, DOXIL® [[doxil]] could not be confirmed to be bioavailable to cell culture cells. Thus, agents which initially screened as statistically negative may be reflective of formulations that are not readily bioavailable to cell culture cells or may be reflective of the limited dose range or exposure time.

Please amend the paragraph beginning on page 73, line 3 as follows:

D. Endotracheal administration of $10^{11}$ AV2FLAG-luc rAAV particles to male Balb/c mice in conjunction with intravenous administration of DOXIL® [[Doxil]] (dosed in a range of 2, 10, or 20 mg/kg), a liposomal preparation of doxorubicin, to mice enhanced AV2FLAG-luc transduction by 2 logs by day 7 at the 20 mk/kg dose of DOXIL® [[doxil]]. Specifically, at 20 mg/kg DOXIL® [[doxil]], transduction was enhanced on the average of 67-fold by day 7 and 4-fold by day 30. It is worth noting that DOXIL® [[doxil]] previously tested negative in cell line screening while the free compound doxorubicin tested positive in cell line screening (Figures 1A-E ). Liposomal formulations have desirable properties for *in vivo* use including their increased stability or circulation half life making them more bioavailable *in vivo*. Those same characteristics make liposomal formulations less desirable for *in vitro* screening as described above. Thus, one skilled in the art can design formulation strategies for agents of the invention to tailor them to the desired application. In addition to formulation design, one skilled in the art can tailor routes of delivery in order to maximize rAAV transduction efficiencies.

Please amend the paragraph beginning on page 73, line 18 as follows:

In additional experiments, a pseudotyped rAAV vector encoding FVIII was tested in male Rag-1 mice. Rag-1 mice were used because as described in the art, normal mice produce inhibitors of human FVIII that can obscure protein detection in the serum. Rag-1 mice are known to be deficient in the pathways necessary to produce these inhibitors and thus will either produce no inhibitors, lower levels of inhibitors or have extended time periods for development of inhibitors. The rAAV vector was constructed containing serotype 5 capsid proteins and 5'-3' ITRs of AAV-2 flanking a heterologous transgene comprised of the minimal liver specific element HNF3/EBP and a human B-domain deleted FVIII gene (a second construct was identical except it contained a B-domain deleted canine FVIII gene). Animals were administered $10^{12}$ rAAV vector particles intravenously via the lateral teil vein concurrently with 20 mg/kg of DOXIL® [[doxil]] at day 0. Circulating, bioavailable FVIII activity was measured from the serum at days 31, 53 and 90 by techniques known in the art including ELISA and Coatest. Data presented in Figure 3 demonstrate that animals not treated with DOXIL® [[doxil]] had barely detectable levels of FVIII in the range of 0.99 ng/ml for days 31 and 53 which decreased to 0.13 ng/ml by day 90. In contrast, animals dosed with 20 mg/kg of DOXIL® [[doxil]] had over 40 times the levels of FVIII protein. Interestingly, the decline in FVIII protein seen in animals not treated with DOXIL® [[doxil]] at day 90 (0.13 ng/ml) was not evident in animals treated with DOXIL® [[doxil]] (40.16 ng/ml) indicating that DOXIL® [[doxil]] not only enhanced rAAV transduction as evident at the shorter time period, but the agent of the invention also prolonged expression. In order to demonstrate that DOXIL® [[doxil]] was affecting rAAV transduction and not merely affecting the FVIII protein translation or stability, RS-PCR was performed on liver tissue at the day 53 time point. The data presented for individual animals in Table 1 demonstrates that the increase in FVIII protein noted in animals treated with DOXIL® [[doxil]] correlates with the levels of mRNA detected.

Please amend the paragraph beginning on page 74, line 13 as follows:

The increase *in vivo* rAAV transduction produced by DOXIL® [[doxil]] was further confirmed utilizing the same vectors and protocol described above in male FVIII knockout mice tolerized to the human FVIII protein utilizing a cytoxan mediated tolerization strategy as described in the art. Animals were treated with weekly injection of 50 mg/kg cytoxan beginning at the time of rAAV vector delivery. Data presented in Table 2 confirmed the previously described results when tested by ELISA or Coatest at days 14 and 25, namely animals dosed with DOXIL® [[doxil]] demonstrated at least a ten-fold enhancement of rAAV transduction.